O3 February 2004

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Amendments to the Specification:

1AP20 Rect FCT/FTO 19 APR 2006

Please insert the following heading and paragraph as the first paragraph on the first page in the application:

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a 371 National Phase Entry Application of co-pending International Application PCT/US2004/003020, filed February 3, 2004, which designated the U.S. and claims the benefit under 35 U.S.C §119(e) of U.S. Provisional Application No. 60/444,475, filed February 3, 2003; the contents of which are herewith incorporated by reference in their entirety.

Please replace paragraph [0014] and [0015] on pages 4 and 5, and replace it with the following amended paragraphs:

[0014] Figures 1A and B demonstrate alignments of the predicted amino acid sequences of human and zebrafish proteins. Figure 1A shows human ANX2 (SEQ ID NO: 1) versus zebrafish ANX2b (SEQ ID NO: 2). Sequence similarity is 72%. Figure 1B shows human CAV1 (SEQ ID NO: 3) versus zebrafish CAV1 (SEQ ID NO: 4). Sequence similarity is 82%.

[0015] Figures 2A-E demonstrate expression of CAV1 and ANX2. Figure 2A shows a comparison of human and zebrafish chromosomal segments and reveals synteny between cav1 and anx2 orthologues. Figure 2B shows expression of cav1 and anx2b in zebrafish larvae. Embryos were fixed in 4% paraformaldehyde and probed with digoxigenin-labeled antisense RNA as described in (22). Top, lateral views of embryos probed for anx2b at 48 hpf (left) and 96 hpf (right). Note strong expression in the epithelium. Scale bar: 500 μm. Bottom, lateral views of embryos probed for cav1 at 48 hpf (left) and 96 hpf (right). Expression is concentrated in the intestinal epithelium, but cav1 can also be seen in the somite boundaries at 48 hpf (left, arrowhead) and in the heart ventricle (96 hpf). Scale bar: 500 μm. Figure 2C shows identification of a CAV-ANX2b heterocomplex. Equal amounts of protein (20 μg) isolated from adult fish or adult fish intestine were resolved by SDS-PAGE and immunoblotted with ANX2 IgG or CAV1 IgG. The data are representative of 5 independent experiments. Figure 2D shows equal amounts of protein (20 μg) isolated from the aorta or

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intestine of C57BL/6 mice that were resolved by SDS-PAGE and immunoblotted with ANX2 IgG or CAV1 IgG. The data are representative of three independent experiments. Figure 2E (SEQ ID NOS 5-9 respectively, in order of appearance) shows the approximately 55 kDa band immunoprecipitated from adult intestine using CAV1 IgG as described previously (9) and resolved by SDS-PAGE. The 55 kDa band was recovered from the gel, digested with trypsin and the resulting fragments resolved by SDS-PAGE and transferred to nylon membrane. Five of the fragments were sequenced by mass spectrometry. The sequence of each fragment is shown along with the region to which they correspond in CAV1 or ANX2b. The letter "X" signifies an unidentified amino acid residue.